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| 09/500,713      | 02/09/2000  | James R. Connor      | 98-2046             | 2989             |

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EXAMINER

CHERNYSHEV, OLGA N

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1646

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/500,713

Applicant(s)

CONNOR ET AL.

Examiner

Olga N. Chernyshev

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-17,19 and 23-27 is/are pending in the application.
- 4a) Of the above claim(s) 11-16 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 27 is/are allowed.
- 6) ☒ Claim(s) 1,3-10,17,19 and 23-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 01, 2003 has been entered.

### ***Response to Amendment***

2. Claims 26 and 27 have been added as requested in the amendment, filed on October 01, 2003. Claims 1, 3-17, 19 and 23-27 are pending in the instant application.

Claims 11-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made without traverse in Paper No. 7.

Claims 1, 3-10, 17, 19 and 23-27 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on October 01, 2003 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-10, 17, 19 and 23-25 and newly submitted claim 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1 and 17 are directed to a method for the detection of multiple sclerosis (MS) by comparing the degree of binding of iron binding protein with two brain tissue samples, a first brain tissue sample from a human suspected of having a demyelinating disease and a second normal brain tissue sample, wherein a difference in said binding confirms a detection of multiple sclerosis in first tissue sample. Claims 3-10 and 19 and 23-25 are dependent claims. Claims 1, 3-10, 17, 19 and 23-26 lack enablement because it is not clear what difference or degree of difference is indicative of multiple sclerosis. The instant specification, as filed fails to provide a clear definitive explanation what is a critical feature that allows for diagnosis of MS. Applicant traverses the rejection on the premises that the instant specification, as filed, teaches “how *any* difference in the degree of binding of an iron binding protein, between an experimental and control brain tissue sample, confirms the detection of multiple sclerosis in said experimental brain tissue sample” (page 6, section 1 of the Response). Applicant also submits that “the Examiner is not considered (under law) “one skilled in the art”, and further urges the Examiner

to provide an affidavit to support the instant rejection because, according to Applicant, it “is based on facts within the personal knowledge of the examiner” (beginning at page 7 of the Response). These arguments have been fully considered but are not deemed to be persuasive for the following reasons.

Because the instant rejection is not “based on facts within the personal knowledge of the examiner”, no affidavit to support the rejection will be provided. The instant rejection is based solely on the analysis of the claims “in the light of the specification” (page 6, section 1 of the Response). As such, according to the instant specification on page 8, second paragraph,

“Applicants demonstrate the distribution of ferritin binding is opposite of that seen for the distribution of the transferrin receptor in normal adult human brain (predominantly found in gray matter). Applicants demonstrate the normal distributions of transferrin and ferritin binding sites are altered in and around plaques from periventricular white matter isolated from multiple sclerotic (MS) brains. In direct contrast to ferritin binding, transferrin binding in the JS tissue can be seen in white matter periplaque regions and to varying degrees within the lesion itself. The transferrin binding in the periplaque region is to oligodendrocytes as indicated by immunocytochemistry for the transferrin receptor”.

Further, on page 22, Example 10 provides a disclosure of specific differences in “Binding Distributions Of Ferritin And Transferrin”.

“Figure 4 shows the results of binding distributions for 125I rH-ferritin and 125I human holo transferrin to contiguous sections from two regions of normal control brains. Ferritin binding distribution is primarily within white matter tracts in both cortex and cerebellum. Transferrin binding distribution is evident primarily within gray matter.

A total of 4 different brains containing MS lesions were examined. In non-lesion areas 1251 rH-ferritin binding was present in white matter regions and 1251 transferrin binding was primarily in grey matter areas. However, in lesion containing white matter, 1251 transferrin bound to the periplaque region. 1251 rH-ferritin binding was not present in the periplaque region or within the lesion itself. Indeed the distributions of transferrin and ferritin binding in white matter periplaque regions were non-overlapping. Figure 5 shows the binding distributions of 1251 rH-ferritin and 1251 human holo transferrin to representative tissue sections from the brain of a multiple sclerosis (MS) patient. The binding pattern returned to normal in the white matter as the distance from the lesion became greater. Transferrin binding surrounding the plaque area is evident only at the edges of the lesion, whereas no ferritin binding activity is present in the lesion or in the periplaque region”.

Thus, Applicant invention is predicated on the finding of differences in binding of ferritin and transferrin between normal and multiple sclerosis (MS) brain tissue. Applicant further extrapolates this finding into the method for the detection of MS. However, the claims, as written, fail to provide any definitive description of what is considered to be a specific point of reference indicative of MS. Is it a difference in intensity of binding, or is it difference in specific location of binding, such as binding of transferrin to periplaque region indicative of MS, as recited in claim 27, for example? Applicant’s argument that “*any* difference in degree of binding” confirms the detection of MS (page 6, section 1 of the Response) is not persuasive because the instant specification, as filed, does not disclose any numeral value of degree of binding of ferritin or transferrin. On the contrary, it appears that that the degree of binding is time dependent and varies between the samples (see Figure 1 and description on page 4 of the

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instant specification), which only confirms the Examiner's position that "one skilled in the art would reasonably assume that any two brain tissue samples even from two normal unaffected individuals would display some differences in binding of iron binding protein, or, in another words, would not be completely identical in the pattern of binding distribution" (see section 5 of the previous office action of Paper No. 20).

The Declaration of Connor under 37 CFR 1.132 filed October 01, 2003 is insufficient to overcome the instant rejection because it addresses mainly the issue of no "significant differences were seen in the distribution of iron binding between (control) tissue obtained from different individuals (e.g. surgical patients vs. cadavers) free from the pathological manifestations of a demyelinating disease" (section 3 of the Declaration). However, the Examiner has never disputed this issue. The question at hand, however, remains, what is the critical point of reference that is indicative of MS? Or, what is the minimal value of degree of binding that is indicative of MS? According to the instant specification, some variation in distribution of iron binding exists, see the use of error marks in Figure 1, for example, and also statement regarding "significant differences" in Declaration of Connor (see above). If any difference in binding is indicative of MS, how the distinction between control samples was made?

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc. v. Novo Nordisk*, 42 USPQ 2d 100, (CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere

germ of an idea does not constitute enabling disclosure”. The court further stated that “when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art”, “[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement”.

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is indefinite for recitation of “decreased ferritin binding” without providing a point of reference to which the comparison of ferritin binding is supposed to be made.

### ***Conclusion***

8. Claims 1, 3-10, 17, 19 and 23-26 are rejected. Claim 27 is allowed.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

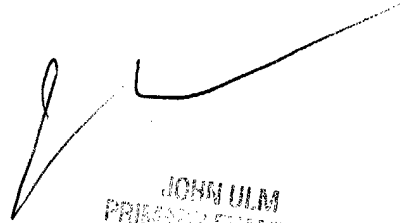
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Olga N. Chernyshev, Ph.D.  
December 11, 2003

OC

  
JOHN ULM  
PRIMARY EXAMINER  
GROUP 1800